IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of	Examiner: Gabel, Gailene
RAO Galla Chandra, LARSON Christopher, REPOLLET Madeliine, RUTNER Herman, TERSTAPPEN Leon, O'HARA Shawn Mark and GROSS, Steven	Group Art Unit: 1641
Serial No. 10/780,399	Response to 06/15/2007 Office Action
Filed: 02/17/2004	
For: ANALYSIS OF CIRCULATING TUMOR CELLS, FRAGMENTS, AND DEBRIS	Our File No.: IMMC 308 PCT/US

Remarks

Applicants have rewritten the claims to define the invention more particularly and distinctly so as to overcome the technical rejections and define the invention's patentability over the prior art.

Specification

All spelling and trademark errors have been corrected as shown in the amendments below.

Claim Rejection- 35 USC §112

Claim 44 and claim 53, element (b) have been amended to specify magnetic labeling as intact malignant cells, cell fragments and cellular debris.
Claim 44 and claim 53, element (c) have been amended to again specify magnetic labeling and to provide an essential element (i.e. the specific binding pair) needed to label the intact cells.

Claim 44 and claim 53, element (d) have been amended to reflect the monitoring focus in the preamble whereby a change in the sample components is assessed over time.

35 USC 102

5. Claims 44-61 are rejected as anticipated by Schmitz et al. (US 6,190,870)

Schmitz et al rely on HGMS using an internal magnet (Miltenyi Biotec GmbH), coupled with the use of conventional density gradients, for separation of the intact target cells. The method requires the use of a ferromagnetic matrix followed by flow cytometric enumeration and as described in Example 4 of US 6,190,870 further incorporates the use of filters. Schmitz et al does not discuss, nor appreciate, additional considerations in the combined analysis of intact cells, debris, and fragments.

In order to classify and assess diagnostic relevance, the present invention appreciates the importance of maintaining the integrity of the sample so as to not adversely affect the classifiable tumor cells and stainable debris [0006]. The present invention utilizes, in part, an external arrangement of magnets to allow for improved visualization and confirmation of the intact cells, debris, or fragments [0008]. Damaged cells may have large pores allowing leakage of the liquid and particulate cytosolic contents (relevant in debris/fragment analysis). This leakage results in a change in the buoyant densities well above densities of RBC [0014]. So the use of filters, density gradients and a ferromagnetic matrix suggests that Schmitz et al could not appreciate the problems in processing a sample to obtain images of damaged or fragmented CTC's in assessing disease where it would be possible that the damage occurred during subsequent processing, and thus artifactual.

6. Claims 44-61 are rejected as anticipated by Fodstad et al. (US 6,265,229)

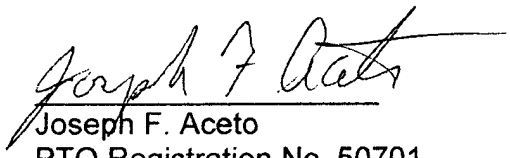
For all the reasons presented in #5, applicant respectfully suggests that Fodstad et al would be unable to assess intact malignant cells, cell fragments, cell debris, and cell clusters in monitoring malignancy. Artifacts from damaged

CTC in processing and other artifactual considerations not appreciated or discussed in Fodstad et al would inhibit the effective analysis of intact malignant cells, cell fragments, cell debris, and cell clusters in the present invention.

Applicants have amended claim 44 and claim 53 to reflect the artifactual processing considerations and limit the method to the application of an external magnetic field to the sample.

By the attached amendments, applicants have amended the claims to define the invention more particularly and distinctly so as to overcome the rejections and to patentably define the invention over the prior art. In view of these amendments and related discussions and arguments, it is respectfully urged that the rejections be withdrawn and that this application be passed to issue. In the event the examiner has any comments or questions, the examiner is invited to telephone or e-mail applicants' undersigned representative at the number below.

Yours Very Respectfully,



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